Biol Blood Marrow Transplant 20 (2014) 1815–1827

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

ASBMT American Society for Blood and Marrow Transplantation

Hospital Length of Stay in the First 100 Days after Allogeneic Hematopoietic Cell Transplantation for Acute Leukemia in Remission: Comparison among Alternative Graft Sources

Karen K. Ballen [1], Steven Joffe [2], Ruta Brazauskas [3,4], Zhiwei Wang [3], Mahmoud D. Aljurf [5], Görgün Akpek [6], Christopher Dandoy [7], Haydar A. Frangoul [8], César O. Freytes [9], Nandita Khera [10], Hillard M. Lazarus [11], Charles F. LeMaistre [12], Paulette Mehta [13,14], Susan K. Parsons [15], David Szwajcer [16], Celalettin Ustun [17], William A. Wood [18], Navneet S. Majhail [19,*]

[1] *Department of Hematology/Oncology, Massachusetts General Hospital, Boston, Massachusetts*
[2] *Department of Medical Ethics and Health Policy, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania*
[3] *Center for International Blood and Marrow Transplant Research, Department of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin*
[4] *Division of Biostatistics, Institute for Health and Society, Medical College of Wisconsin, Milwaukee, Wisconsin*
[5] *Department of Oncology, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia*
[6] *Department of Oncology, Banner M.D. Anderson Cancer Center, Gilbert, Arizona*
[7] *Department of Hematology/Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio*
[8] *Department of Pediatric Hematology/Oncology, Vanderbilt University Medical Center, Nashville, Tennessee*
[9] *Hematopoietic Stem Cell Transplant Program, South Texas Veterans Health Care System and University of Texas Health Science Center San Antonio, San Antonio, Texas*
[10] *Department of Hematology/Oncology, Mayo Clinic Arizona and Phoenix Children's Hospital, Phoenix, Arizona*
[11] *Department of Medicine, Seidman Cancer Center, University Hospitals Case Medical Center, Cleveland, Ohio*
[12] *Hematology and Bone Marrow Transplant, Sarah Cannon, Nashville, Tennessee*
[13] *Central Arkansas Veterans Healthcare System, Little Rock, Arkansas*
[14] *University of Arkansas for Medical Sciences, Little Rock, Arkansas*
[15] *Department of Medicine and Pediatrics, Tufts Medical Center, Boston, Massachusetts*
[16] *Department of Hematology, CancerCare Manitoba, University of Manitoba, Winnipeg, Manitoba, Canada*
[17] *Divison of Hematology, Oncology and Transplantation, University of Minnesota Medical Center, Minneapolis, Minnesota*
[18] *Department of Hematology/Oncology, University of North Carolina Hospitals, Chapel Hill, North Carolina*
[19] *Blood and Marrow Transplant Program, Cleveland Clinic, Cleveland, Ohio*

Article history:
Received 27 May 2014
Accepted 15 July 2014

Key Words:
Hematopoietic cell transplantation
Umbilical cord blood
Leukemia
Length of stay
Resource utilization

A B S T R A C T

Several studies have shown comparable survival outcomes with different graft sources, but the relative resource needs of hematopoietic cell transplantation (HCT) by graft source have not been well studied. We compared total hospital length of stay in the first 100 days after HCT in 1577 patients with acute leukemia in remission who underwent HCT with an umbilical cord blood (UCB), matched unrelated donor (MUD), or mismatched unrelated donor (MMUD) graft between 2008 and 2011. To ensure a relatively homogenous study population, the analysis was limited to patients with acute myelogenous leukemia and acute lymphoblastic leukemia in first or second complete remission who underwent HCT in the United States. To account for early deaths, we compared the number of days alive and out of the hospital in the first 100 days post-transplantation. For children who received myeloablative conditioning, the median time alive and out of the hospital in the first 100 days was 50 days for single UCB recipients, 54 days for double UCB recipients, and 60 days for MUD bone marrow (BM) recipients. In multivariate analysis, use of UCB was significantly associated with fewer days alive and out of the hospital compared with MUD BM. For adults who received myeloablative conditioning, the median time alive and out of the hospital in first 100 days was 52 days for single UCB recipients, 55 days for double UCB recipients, 69 days for MUD BM recipients, 75 days for MUD peripheral blood stem cell (PBSC) recipients, 63 days for MMUD BM recipients, and 67 days for MMUD PBSC recipients. In multivariate analysis, UCB and MMUD BM recipients had fewer days alive and out of the hospital compared with recipients of other graft sources. For adults who received a reduced-intensity preparative regimen, the median time alive and out of the hospital during the first 100 days was 65 days for single UCB

Financial disclosure: See Acknowledgments on page 1826.

* Correspondence and reprint requests: Navneet S. Majhail, MD, Blood and Marrow Transplant Program, Cleveland Clinic, 9500 Euclid Ave, R35, Cleveland, OH 44195.

E-mail address: majhain@ccf.org (N.S. Majhail).

http://dx.doi.org/10.1016/j.bbmt.2014.07.021

recipients, 63 days for double UCB recipients, 79 days for MUD PBSC recipients, and 79 days for MMUD PBSC recipients. Similar to the other 2 groups, receipt of UCB was associated with a fewer days alive and out of the hospital. In conclusion, length of stay in the first 100 days post-transplantation varies by graft source and is longer for UCB HCT recipients. These data provide insight into the resource needs of patients who undergo HCT with these various graft sources.

INTRODUCTION

The use of alternative donors, such as unrelated umbilical cord blood (UCB), haploidentical family members, and mismatched unrelated donors (MMUDs), allows patients without an HLA-matched sibling or matched unrelated donor (MUD) to proceed to hematopoietic cell transplantation (HCT). Several studies have shown comparable HCT survival outcomes with different graft sources [1-7]; however, data are limited on the costs and resource needs of HCT performed using different graft sources.

Allogeneic HCT is a resource-intensive procedure, and health care resource allocation is now being analyzed closely. Khera et al. [8] and Preussler et al. [9] recently summarized the trends in costs of HCT. In a study using a national claims database of commercially insured population in the United States, Majhail et al. [10] reported median costs associated with allogeneic HCT of $203,026 in the first 100 days post-transplantation. The median total hospital length of stay (LOS) was 31 days, with the initial transplantation hospitalization accounting for >75% of these early costs. Data on costs and resource needs by graft source were not available. The Minnesota group compared HCT-associated costs in the first 100 days between UCB recipients and matched related donor graft recipients who received pretransplantation conditioning with either a myeloablative conditioning (MAC) or reduced-intensity conditioning (RIC) regimen [11,12]. The median cost per day of survival (not including graft acquisition) was $1016 for MAC matched related donor recipients, $2082 for MAC UCB recipients, $612 for RIC matched related donor recipients, and $1156 for RIC UCB recipients. In a separate study, the same group reported greater blood product use in patients receiving UCB grafts and patients receiving a MAC regimen [13].

Information on the resource needs associated with the different alternative graft sources obtained through a multicenter study will have important policy implications for estimating costs and needs for resources, infrastructure, and personnel. Previous studies of the costs associated with HCT have been limited to single-center analyses and reflect institutional practices specific to that institution. Furthermore, resource utilization in this population has not been well described. Although the Center for International Blood and Marrow Transplant Research (CIBMTR) does not collect data on resource utilization and costs of HCT, it does capture information on the total hospital LOS in the first 100 days. Given that hospitalization is the largest contributor to early post-transplantation resource utilization, we compared LOS in the first 100 days in recipients of different graft sources in a multicenter cohort. This information can aid transplantation physicians and centers in planning for resource allocation and utilization such as for hospital beds and admissions.

PATIENTS AND METHODS

Data Source and Patients

The CIBMTR comprises a voluntary working group of more than 500 transplantation centers worldwide that contribute detailed data on consecutive allogeneic and autologous HCT to a statistical center at the Medical College of Wisconsin in Milwaukee and the National Marrow Donor Program's Coordinating Center in Minneapolis. Participating centers are required to report all transplantations consecutively; compliance is monitored by onsite audits. Patients are followed longitudinally, with yearly follow-up. Computerized checks for errors, physicians' review of submitted data, and onsite audits of participating centers ensure data quality. Observational studies conducted by the CIBMTR are performed in compliance with the HIPAA Privacy Rule as a public health authority and in compliance with all applicable federal regulations pertaining to the protection of human research participants as determined by continuous review of the National Marrow Donor Program's Institutional Review Board.

The study population comprised patients with acute myelogenous leukemia (AML) or acute lymphoblastic leukemia (ALL) in first or second complete remission (CR) who underwent their first allogeneic HCT in the United States and were reported to the CIBMTR between 2008 and 2011. All age groups and recipients of both MAC and RIC regimens were considered. Graft sources included UCB and both 7/8 HLA-MMUD and 8/8 HLA-MUD bone marrow (BM) and peripheral blood stem cells (PBSCs); HLA-matched sibling donors were excluded. Owing to the small number of patients, haploidentical HCT recipients were not included in this analysis. To obtain a relatively homogenous group for comparison, we restricted our study population to commonly used conditioning regimens. MAC regimens included busulfan (Bu) + cyclophosphamide (Cy) ± other and Cy + total body irradiation (TBI) ± other. RIC regimens included TBI + Cy + fludarabine (Flu) ± other, TBI + Flu ± other (no Cy), Bu + Flu ± other, and melphalan (Mel) + Flu ± other. For the same reason, we excluded patients who had received ex vivo T cell depletion as part of graft-versus-host disease (GVHD) prophylaxis.

Outcomes and Study Definitions

The primary objective of this study was to compare LOS in recipients of HCT from different graft sources. LOS is captured by the CIBMTR as total days of hospitalization (initial admission and any readmissions) between day 0 (day of transplantation) and day +100 post-transplantation. Patients who die early after transplantation have less time at risk for hospitalization and a shorter LOS than those who survive to day +100. To account for this association of early mortality with shorter hospitalization, in our analysis we used the number of days alive and out of the hospital as the metric for comparing LOS in first 100 days. For patients who died within 100 days, we evaluated the number of days of survival out of the hospital; for example, the number of days alive and out of the hospital would be 0 days for a patient who died on day +20 and had spent all 20 days in the hospital and 20 days for a patient who died on day +40 and had spent 20 days in the hospital. For patients who survived through day 100, we censored follow-up at that time point; for example, the number of days alive and out of the hospital would be 80 days for a patient who survived through day +100 and had spent 20 days in the hospital. We also evaluated the proportion of days alive and out of the hospital; the results for both analyses were similar, and thus we present data only on the number of days alive and out of the hospital. In addition, we performed a subset analysis in patients who survived through day +100. We also report 100-day overall survival in recipients of the various graft sources. All outcomes were assessed from the date of HCT.

Given the differences in patient characteristics and transplantation practices among adult and pediatric transplantation centers, We analyzed pediatric (age ≤18 years) and adult (age >18 years) transplant recipients separately. We also analyzed MAC and RIC regimen recipients separately, given the variation in the time to neutrophil engraftment and consequently LOS. We excluded patient groups with a sample size of <30 patients. Specifically, we excluded pediatric patients who received an RIC regimen, recipients of haploidentical transplants, and recipients of some graft source subcategories (eg, pediatric MUD PBSC, pediatric MMUD BM and PBSC, and adult RIC MUD and MMUD BM). Thus, our final study population comprised 1577 patients, who were analyzed in 3 separate groups: pediatric MAC HCT recipients (single UCB, double UCB, and MUD BM), adult MAC HCT recipients (single UCB, double UCB, MUD BM, MUD PBSC, MMUD BM, and MMUD PBSC), and adult RIC HCT recipients (single UCB, double UCB, MUD PBSC, and MMUD PBSC).

Table 1
Patient Characteristics

Characteristic	Pediatric, MAC Regimen				Adult, MAC Regimen							Adult, RIC Regimen				
	Single UCB	Double UCB	MUD BM	*P* value	Single UCB	Double UCB	MUD BM	MUD PBSC	MMUD BM	MMUD PBSC	*P* value	Single UCB	Double UCB	MUD PBSC	MMUD PBSC	*P* value
Number of patients	219	80	69		65	146	92	297	42	126		16	188	160	77	
Number of centers	54	32	30		19	45	38	68	25	53		9	43	48	36	
Age at transplantation, yr, median (range)	6 (<1-18)	12 (1-18)	9 (<1-18)	<.001	45 (18-72)	33 (18-68)	41 (18-63)	42 (19-66)	35 (18-61)	41 (19-65)	<.01	58 (19-70)	58 (19-72)	63 (21-78)	61 (23-73)	<.01
Male sex	114 (52)	54 (68)	41 (59)	.05	25 (38)	72 (49)	48 (52)	146 (49)	21 (50)	66 (52)	.57	8 (50)	94 (50)	104 (65)	43 (56)	.04
Recipient race											<.01					<.01
White	172 (79)	64 (80)	57 (83)	.01	48 (74)	106 (73)	86 (93)	276 (93)	36 (86)	110 (87)		13 (81)	153 (81)	154 (96)	68 (88)	
Black	26 (12)	7 (9)	2 (3)		9 (14)	24 (16)	2 (2)	6 (2)	4 (10)	8 (6)		2 (13)	13 (7)	2 (1)	5 (6)	
Other	11 (5)	8 (10)	2 (3)		7 (11)	13 (9)	2 (2)	11 (4)	1 (2)	7 (6)		1 (6)	18 (10)	0	2 (3)	
Unknown	10 (5)	1 (1)	8 (12)		1 (2)	3 (2)	2 (2)	4 (1)	1 (2)	1 (1)		0	4 (2)	4 (3)	2 (3)	
Karnofsky/Lansky score ≥80	209 (95)	79 (99)	67 (97)	.34	57 (88)	137 (94)	86 (93)	260 (88)	42	116 (92)	.13	12 (75)	176 (94)	151 (94)	63 (82)	<.01
Diagnosis				<.01							.02					.08
AML	88 (40)	35 (44)	46 (67)		44 (68)	94 (64)	70 (76)	236 (79)	30 (71)	94 (75)		14 (88)	160 (85)	148 (93)	72 (94)	
ALL	131 (60)	45 (56)	23 (33)		21 (32)	52 (36)	22 (24)	61 (21)	12 (29)	32 (25)		2 (13)	28 (15)	12 (8)	5 (6)	
Disease status				.08							.12					.10
CR1	111 (51)	34 (43)	42 (61)		45 (69)	87 (60)	61 (66)	217 (73)	27 (64)	85 (67)		13 (81)	131 (70)	129 (81)	60 (78)	
CR2	108 (49)	46 (58)	27 (39)		20 (31)	59 (40)	31 (34)	80 (27)	15 (36)	41 (33)		3 (19)	57 (30)	31 (19)	17 (22)	
HCT-CI score				.07							.29					.09
0	178 (81)	61 (76)	48 (70)		22 (34)	59 (40)	30 (33)	107 (36)	21 (50)	51 (40)		8 (50)	53 (28)	55 (34)	16 (21)	
1-2	29 (13)	15 (19)	11 (16)		16 (25)	49 (34)	34 (37)	94 (32)	6 (14)	45 (36)		3 (19)	68 (36)	48 (30)	23 (30)	
≥3	12 (5)	4 (5)	10 (14)		27 (42)	38 (26)	28 (30)	95 (32)	15 (36)	30 (24)		5 (31)	67 (36)	57 (36)	38 (49)	
Unknown	0	0	0		0	0	0	1 (<1)	0	0		0	0	0	0	
Time from diagnosis to HCT, mo, median (range)	8 (<1-82)	10 (3-62)	6 (2-108)	.18	7 (<1-135)	7 (2-70)	6 (3-168)	6 (<1-177)	7 (3-54)	7 (2-86)	.06	5 (2-49)	7 (2-313)	6 (2-58)	7 (2-36)	.20
Conditioning regimen				<.01							<.01					<.01
Bu + Cy ± other	46 (21)	7 (9)	28 (41)		13 (20)	16 (11)	34 (37)	118 (40)	15 (36)	48 (38)		-	-	-	-	
TBI + Cy ± other	173 (79)	73 (91)	41 (59)		52 (80)	130 (89)	58 (63)	179 (60)	27 (64)	78 (62)		-	-	-	-	
TBI + Cy + Flu ± other	-	-	-		-	-	-	-	-	-		9 (56)	152 (81)	1 (1)	0	
TBI + Flu ± other (no Cy)	-	-	-		-	-	-	-	-	-		0	2 (1)	30 (19)	21 (27)	
Bu + Flu ± other	-	-	-		-	-	-	-	-	-		1 (6)	1 (1)	101 (63)	42 (55)	
Mel + Flu ± other	-	-	-		-	-	-	-	-	-		6 (38)	33 (18)	28 (18)	14 (18)	
TBI conditioning	173 (79)	73 (91)	41 (59)	<.01	52 (80)	130 (89)	58 (63)	179 (60)	27 (64)	78 (62)	<.01	9 (56)	154 (82)	31 (19)	21 (27)	<.01
CMV status*				<.01							<.01					<.01
Donor and recipient negative	51 (23)	14 (18)	23 (33)		10 (15)	26 (18)	31 (34)	90 (30)	10 (24)	41 (33)		4 (25)	25 (13)	46 (29)	12 (16)	
Donor or recipient positive	138 (63)	48 (60)	45 (65)		49 (75)	99 (68)	58 (63)	203 (68)	32 (76)	84 (67)		10 (63)	126 (67)	112 (70)	62 (81)	
Unknown	30 (14)	18 (23)	1 (1)		6 (9)	21 (14)	3 (3)	4 (1)	0	1 (1)		2 (13)	37 (20)	2 (1)	3 (4)	
ATG before transplantation	75 (34)	11 (14)	26 (38)	<.01	47 (72)	132 (90)	79 (86)	238 (80)	27 (64)	81 (64)	<.01	8 (50)	131 (70)	78 (49)	39 (51)	<.01
Household income, $ (× 1000), median (range)†	52 (16-150)	51 (14-166)	48 (24-155)	.47	61 (22-157)	52 (17-141)	53 (20-134)	57 (14-143)	53 (24-151)	54 (22-181)	.11	65 (20-106)	55 (20-184)	60 (22-166)	55 (24-127)	.42

* For double UCB recipients, donor is classified as CMV seropositive if either of the 2 units was CMV positive.
† Based on ZIP code of patient residence, from the 2011 US Census American Community Survey data.

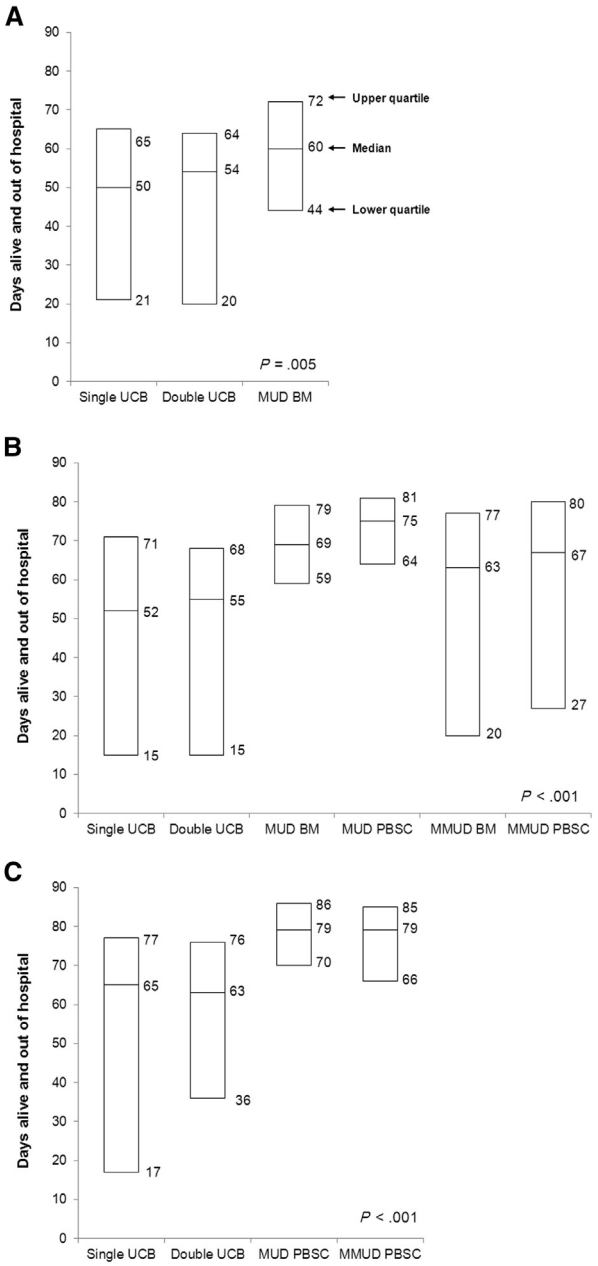

Figure 1. Number of days alive and out of the hospital in the first 100 days after allogeneic transplantation. (A) Pediatric MAC HCT recipients. (B) Adult MAC HCT recipients. (C) Adult RIC HCT recipients. The lower and upper bars represent the IQR (25th-75th percentile), and the middle bar represents the median.

Patient ethnicity (Hispanic or non-Hispanic) and race (white, black, Asian, American Indian/Alaska Native, Native Hawaiian/other Pacific Islander) are reported to the CIBMTR by transplantation centers according to the US Office of Management and Budget classification [14-16]. Preparative regimens were classified as MAC or RIC according to CIBMTR criteria [17,18]. HLA matching was performed at low resolution for class I and at high resolution for class II for UCB HCT, as are the majority of UCB transplants performed in this era. In patients receiving a double-unit UCB transplant, the worst match to the patient between the 2 units was used to categorize the degree of recipient–UCB unit match. For MMUD and MUD HCT recipients, high-resolution typing at HLA-A, -B, -C and -DRB1 was used.

Statistical Analysis

Summaries of patient-, disease-, and treatment-related characteristics were generated for the various graft source groups. The chi-square test was used to compare categorical variables, and the Kruskal-Wallis test was used to compare continuous variables. Univariate probabilities of overall survival were calculated using the Kaplan-Meier estimator [19].

Multivariate analysis was performed using Poisson regression. Overall survival and LOS were similar in recipients of single UCB HCT and recipients of double UCB HCT in all 3 groups analyzed, so we combined the 2 categories into a single category in multivariate analyses. We built 2 models. The first model considered the mean time (in days) that patients were alive and out of the hospital within the first 100 days after transplantation. Results are summarized as means ratios for comparing groups; a means ratio >1 indicates more days alive and out of the hospital. The second model examined the proportion of days alive in the first 100 days spent out of the hospital. Results for both models were similar, and thus only the former are presented herein. Logistic regression models were used to assess 100-day mortality, because there was no censoring before 100 days. (Deaths occurring at day +100 were treated as events.)

In addition to graft source, the patient and disease characteristic covariates considered in the multivariate models included age, sex, recipient race, Karnofsky performance status before transplantation, cytomegalovirus (CMV) serologic status, HCT comorbidity index (HCT-CI) score, median household income (imputed by patient ZIP code of residence based on the 2011 US Census American Community Survey data), diagnosis, and disease status at transplantation. Information on patients' insurance coverage was not available and thus was not considered in the analysis.

All computations were performed using the SAS statistical package, version 9.2 (SAS Institute, Cary, NC). All P values are 2-sided. A statistical significance level (α) of 0.05 was used throughout.

RESULTS

Patient Characteristics

Patient characteristics are summarized in Table 1. In the pediatric MAC HCT recipients, there were differences among the single UCB, double UCB, and MUD BM recipients in terms of age, sex, race, diagnosis, CMV serostatus, conditioning regimen, and exposure to antithymocyte globulin (ATG). Double UCB recipients were older and were less likely to receive ATG. Compared with MUD BM recipients, single and double UCB recipients more frequently belonged to nonwhite racial groups and received a TBI + Cy-based conditioning regimen. AML was more frequent in MUD BM recipients compared with UCB recipients. Differences in patient characteristics were seen in the same variables in adult MAC and adult RIC recipients. In adults receiving MAC HCT, UCB recipients were again more frequently nonwhite and more often received a TBI + Cy-based regimen. Similarly, in the adult RIC group, UCB recipients were more often nonwhite. UCB recipients were also younger compared with MUD PBSC and MMUD PBSC recipients. There were notable differences in conditioning regimens, with UCB recipients more likely to have received a TBI + Cy + Flu regimen. There were no significant differences among the various graft sources considered in the 3 cohorts with respect to HCT-CI score or patient socioeconomic status.

For the pediatric MAC group, the median total nucleated cell dose (prefreeze) was 7×10^7/kg recipient weight for single UCB recipients and 8×10^7/kg for double UCB recipients. HLA 4/6-matched units were used in 29% of single UCB and 46% of double UCB HCTs. Among adult MAC recipients of single and double UCB transplants, the corresponding median cell dose was 3×10^7/kg and 5×10^7/kg, respectively, and HLA 4/6-matched units were used in 55% and 68% of recipients, respectively. Among adult RIC recipients, the median prefreeze total nucleated cell dose was 2×10^7/kg in both single and double UCB recipients. Some 44% of single UCB and 57% of double UCB transplants used HLA 4/6-matched units.

Pediatric MAC HCT Group

Figure 1A shows the number of days alive and out of the hospital in the first 100 days after transplantation in

Table 2
Overall Survival at 100 Days, Results of Multivariate Analysis for Overall Mortality and Results of Multivariate Analysis Comparing the Number of Days Alive and Out of the Hospital Among Graft Sources

Category	n	100-Day Survival, % (95% CI)	*P* Value*	OR (95% CI) for 100-Day Mortality	*P* Value†	Means Ratio for Days Alive and Out of Hospital (95% CI)‡	*P* Value§
Pediatric MAC recipients			.09		.28		.03
UCB¶	295	87 (83-91)		1.00		1.00	
MUD BM	69	95 (89-100)		0.55 (0.18-1.63)		1.18 (1.02-1.36)	
Adult MAC recipients			<.001		<.001‖		<.001‖
UCB¶	210	77 (73-83)		1.00		1.00	
MUD BM	92	91 (86-97)		0.33 (0.15-0.73)	.006	1.36 (1.21-1.54)	<.001
MUD PBSC	296	90 (87-93)		0.37 (0.22-0.61)	<.001	1.45 (1.32-1.59)	<.001
MMUD BM	42	76 (64-90)		1.08 (0.49-2.36)	.85	1.06 (0.89-1.26)	.49
MMUD PBSC	126	77 (70-85)		1.04 (0.61-1.77)	.88	1.19 (1.06-1.33)	.003
Adult RIC recipients			.002		<.001‖		<.001‖
UCB¶	204	79 (74-85)		1.00		1.00	
MUD PBSC	160	93 (89-97)		0.25 (0.12-0.50)	<.001	1.38 (1.26-1.52)	<.001
MMUD PBSC	77	87 (80-95)		0.43 (0.19-0.94)	.03	1.33 (1.19-1.48)	<.001

* Log-rank *P* value.
† Logistic regression *P* value.
‡ Means ratio compares the mean number of days that patients were alive and stayed out of the hospital in the first 100 days after transplantation among the graft sources considered and is adjusted for important patient characteristics; a means ratio >1 indicates a better outcome and longer duration alive and out of the hospital; for example, in the pediatric MAC transplant group, recipients of MUD BM on an average, stayed 18% more days alive and out of the hospital compared to UCB recipients.
§ Poisson regression *P* value.
¶ Single and double UCB were combined into a single category because the 100-day survival and days alive and out of the hospital were comparable.
‖ Overall *P* value.

recipients of each of the 3 graft sources compared in this cohort. The median number was 50 days for single UCB, 54 days for double UCB, and 60 days for MUD BM ($P = .005$). Survival at 100 days for single and double UCB HCT recipients was similar (88% [95% confidence interval (CI), 83%-92%] versus 85% [95% CI, 76%-92%]). Given the comparable LOS, the 2 graft sources were combined into a single category for multivariate analysis.

Table 2 presents the results of multivariate analysis. Compared with UCB recipients, MUD BM recipients were alive and out of the hospital for a significantly longer duration in the first 100 days after transplantation (means ratio, 1.18; $P = .03$). We also identified other factors that were significantly associated with total hospital LOS. On average, patients had fewer number of days alive and out of the hospital if they were black (means ratio, 0.75 compared with whites; $P = .01$), had a Karnofsky Performance Status of <80 at HCT (means ratio, 0.63 compared with a score ≥80; $P = .03$) and were CMV seropositive (means ratio, 0.85; $P = .006$).

Table 3 presents days alive and out of hospital by selected patient characteristics, such as recipient race, Karnofsky/Lansky Performance Status at transplantation, HCT-CI score, diagnosis, and median household income.

Overall, 43 patients (12%) died before day +100 (39 UCB recipients; 4 MUD BM recipients), 31 of whom (72%) stayed in the hospital the entire time. Results of logistic regression analysis showed no association between graft source and mortality at 100 days post-transplantation (Table 2). We also performed multivariate analysis for hospital LOS after excluding these 43 patients. In this subset analysis of 100-day survivors, UCB remained associated with fewer days alive and out of the hospital.

Adult MAC HCT Group

We observed significant differences in hospital LOS among patients receiving each of the graft sources compared in this cohort (Figure 1B). The median time alive and out of the hospital in the first 100 days was 52 days for single UCB recipients, 55 days for double UCB recipients, 69 days for MUD BM recipients, 75 days for MUD PBSC recipients, 63 days for MMUD BM recipients, and 67 days for MMUD PBSC recipients ($P <.001$). Single and double UCB recipients had comparable survival at 100 days (74% [95% CI, 63-84%] and 79% [95% CI, 72-85%]); similar to the pediatric analysis, given the similar hospital LOS, here the 2 graft sources also were combined into a single category for multivariate analysis.

Table 2 presents the results of multivariate analysis for this cohort. There was no difference in the number of days alive and out of the hospital between UCB and MMUD BM recipients (means ratio, 1.06; $P = .49$ compared with UCB). However, compared with UCB recipients, the time alive and out of the hospital in the first 100 days was significantly greater for recipients of MUD BM (means ratio, 1.36; $P <.001$), MUD PBSCs (means ratio, 1.45; $P <.001$), and MMUD PBSCs (means ratio, 1.19; $P = .003$). In other pairwise comparisons, MMUD BM recipients had a shorter time alive and out of the hospital than recipients of either MUD BM (means ratio, 0.78; $P = .007$) or MUD PBSCs (means ratio, 0.73; $P <.001$). MMUD PBSC recipients also had fewer days alive and out of the hospital compared with MUD BM (means ratio, 0.87; $P = .03$) and MUD PBSC (means ratio, 0.82; $P <.001$) recipients. There was no significant difference in 100-day LOS between MMUD BM and MMUD PBSC recipients (means ratio, 1.12; $P = .22$) or between MUD BM and MUD PBSC recipients (means ratio, 1.06; $P = .27$). Shorter times alive and out of the hospital were seen in black patients (means ratio, 0.72 compared with whites; $P = .03$) and patients with ALL (means ratio, 0.90 compared with AML; $P = .01$). Patients age ≥25 years at HCT had a shorter LOS compared with those age 18-25 years at HCT (means ratio, 1.18; $P = .001$). Table 3 reports LOS by selected patient characteristics.

One hundered twenty-five patients (16%) died within the first 100 days post-transplantation, of whom 60 (48%) had remained hospitalized the entire time. In logistic regression analysis of 100-day mortality, UCB recipients were significantly more likely than MUD BM and MUD PBSC recipients to die during the first 100 days (Table 2). In multivariate

Table 3
Number of Days Alive and Out of the Hospital in the First 100 Days after Allogeneic HCT by Selected Patient Demographic Factors

Demographic Factor	n	Median Days Alive and Out of Hospital*	IQR	*P* Value†
Pediatric MAC HCT recipients				
Recipient race				.05
White	293	54	32-67	
Black	35	38	0-61	
Other	21	42	17-58	
Unknown	19	53	29-66	
Lansky score at transplantation				.17
≥80	355	53	28-66	
<80	11	19	7-48	
Unknown	2	37	22-52	
HCT-CI score				.99
0	287	52	27-66	
1-2	55	54	16-65	
≥3	26	49	34-63	
Diagnosis				.35
AML	169	54	28-67	
ALL	199	51	22-65	
Median household income, $‡				.98
<50,000	165	53	31-65	
50,000-100,000	167	51	21-67	
≥100,000	20	53	40-61	
Unknown	16	46	34-67	
Adult MAC HCT recipients				
Recipient race				<.001
White	662	70	47-79	
Black	53	48	21-68	
Other	41	66	45-73	
Unknown	12	64	54-80	
Karnofsky score at transplantation				.05
≥80	698	69	44-78	
<80	59	54	38-80	
Unknown	11	80	67-86	
HCT-CI score				.47
0	290	69	41-79	
1-2	244	69	45-79	
≥3	233	68	47-78	
Diagnosis				<.001
AML	568	70	52-79	
ALL	200	60	29-76	
Median household income, $‡				.18
<50,000	294	68	36-77	
50,000-100,000	410	70	52-79	
≥100,000	45	67	32-77	
Unknown	19	68	44-80	
Adult RIC HCT recipients				
Recipient race				.05
White	388	74	54-83	
Black	22	70	43-78	
Other	21	55	21-71	
Unknown	10	72	24-78	
Karnofsky score at transplantation				.008
≥80	402	73	51-82	
<80	33	74	57-85	
Unknown	6	50	48-81	
HCT-CI score				.52
0	132	75	54-83	
1-2	142	73	51-84	
≥3	167	73	50-81	
Diagnosis				.43
AML	394	74	53-83	
ALL	47	70	43-81	
Median household income, $‡				.86
<50,000	159	74	48-85	
50,000-100,000	237	71	53-81	
≥100,000	33	76	59-82	
Unknown	12	74	43-84	

Data by graft source are presented in Figure 1.
* Larger number indicates more days alive and out of the hospital in the first 100 days after transplantation.
† Univariate *P* value.
‡ Based on ZIP code of patient residence (from the 2011 US Census American Community Survey data).

analysis for hospital LOS within the subgroup of patients surviving >100 days, results were similar to the whole cohort, with the number of days alive and out of the hospital for UCB recipients comparable with that of MMUD BM recipients, but significantly less than that of MUD BM, MUD PBSC, and MMUD PBSC recipients.

Adult RIC HCT Group

Figure 1C shows the days alive and out of the hospital for this cohort (median, 65 days for single UCB recipients, 63 days for double UCB recipients, and 79 days for MUD PBSC and MMUD PBSC recipients; $P < .001$). Four patients had no reported inpatient days, presumably because they underwent HCT as an outpatient procedure and did not require subsequent hospitalization within the first 100 days. Here single and double UCB HCT were again combined into 1 category for multivariate analysis because of similar LOS and 100-day survival (75% [95% CI, 52%-92%] and 80% [95% CI, 74%-85%]).

In multivariate analysis, graft source was the sole variable associated with number of days alive and out of the hospital (Table 2). Compared with UCB recipients, the number of days alive and out of the hospital was greater in recipients of MUD PBSCs (means ratio, 1.38; $P < .001$) and MMUD PBSCs (means ratio, 1.33; $P < .001$). There was no difference in hospital LOS between MUD PBSC and MMUD PBSC recipients (means ratio 1.04; $P = .47$). Table 3 reports days alive and out of the hospital by selected patient characteristics for this cohort.

Sixty-four patients (15%) died within the first 100 days, of whom 24 (38%) had remained hospitalized the entire time. Logistic regression analysis revealed an association between graft source and 100-day mortality, with UCB recipients less likely than MUD PBSC and MMUD PBSC recipients to survive to 100 days (Table 2). Results of multivariate analysis of the number of days alive and out of the hospital restricted to the subgroup of 100-day survivors were similar to those seen for the whole cohort.

DISCUSSION

In patients undergoing HCT without an HLA-matched related donor, the decision to use one alternative graft source over another is complex. Transplantation physicians take several factors into consideration in selecting a graft source, including the patient's underlying disease, urgency of

need for transplantation, and donor availability. Little is known about how resource needs compare across alternative graft sources. Using a nationally representative and contemporary cohort of patients, we show that the total hospital LOS in the first 100 days post-transplantation is significantly greater in pediatric and adult recipients of UCB and MMUD HCT compared with recipients of MUD HCT. Although resources generally do not figure directly in decisions about graft source, our data have important policy implications and will inform multiple stakeholders, especially transplantation providers and centers, about the resources needed to care for patients undergoing HCT from alternative graft sources.

Hospital stay is the major driver of early post-transp lantation resource use and costs, with an estimated 75%-95% of total costs in the first 100 days attributed to inpatient stay [9-12,20-25]. We used total LOS in the first 100 days for our analysis (transplantation admission and any subsequent admissions), because these data are captured by the CIBMTR. To account for different rates of early mortality, we used the number of days alive and out of the hospital in the first 100 days as the endpoint of our analysis. Our finding of a longer LOS in UCB recipients may reflect the fact these patients generally demonstrate later engraftment and usually are hospitalized until neutrophil recovery occurs. In the adult MAC HCT group, compared with UCB recipients, MMUD BM recipients had a similar LOS and MMUD PBSC recipients had a shorter LOS. In the adult RIC HCT group, UCB recipients had a longer mean LOS in the first 100 days compared with MMUD PBSC recipients.

LOS, days alive and out of the hospital, and 100-day survival were similar in single and double UCB recipients in our cohort of patients who underwent HCT in the recent era. This likely reflects our understanding, developed over years of research, that centers are able to appropriately select patients for single UCB versus double UCB HCT based on unit cell dose and HLA match, with many centers selecting double UCB HCT if a single UCB unit of adequate cell dose is not available. Our study was not designed to compare outcomes of single versus double UCB HCT. Our results differ from a recently published French study showing a lower relapse rate, improved survival, and increased cost-effectiveness in double UCB HCT compared with single UCB HCT in a cohort of adult patients with acute leukemia [26].

There is considerable interest in comparing outcomes of UCB HCT and haploidentical HCT. Parallel multicenter phase II studies from the Blood and Marrow Transplant Clinical Trials Network have shown a 1-year overall survival of 54% and progression-free survival of 46% after UCB HCT, with corresponding rates of 62% and 48% after haploidentical BM HCT [27]. An ongoing multicenter randomized phase III study through the Network is comparing outcomes between these 2 graft sources. As part of our original study question, we were interested in comparing LOS in UCB HCT and haploidentical HCT; however, we were not able to include haploidentical HCT in our analysis because of the small number of patients. (Only 41 patients reported to the CIBMTR between 2008 and 2011 had received HCT using an “other relative” donor source and met the other study selection criteria.) As more experience with haploidentical HCT is attained, assessment of its associated costs and resource needs compared with other donor sources will be of paramount importance.

An interesting observation is the longer hospital LOS in black children and adults who received MAC conditioning, which persisted even after adjusting for other patient and disease characteristics. Although our study was not designed specifically to study the association of race with outcomes, black pediatric MAC HCT recipients (but not adult recipients) had significantly higher 100-day mortality compared with whites on logistic multivariate regression analysis. It is well known that the use of UCB increases access to HCT, and that UCB is more likely to be used in black patients, who frequently lack other suitable donor sources [28-30]. Previous studies also have shown an association between race and outcomes of allogeneic HCT, including those after single UCB transplantation [15,16,28]. Black recipients of single UCB HCT are also more likely than whites to receive UCB units that are smaller and less well matched [16], which may influence the time to engraftment and consequently the hospital LOS. Thus, such factors as health care disparities and availability of a suitable donor (eg, adequate UCB units) may help explain our finding of a race–hospitalization association. The observation of racial/ethnic differences in LOS requires more detailed examination in future studies.

We considered patient socioeconomic status in our analysis using median household income based on ZIP code of residence. Socioeconomic status is a surrogate for several healthcare status indicators, including insurance status [31]. We did not find an association between socioeconomic status and LOS or 100-day mortality. It is possible that biological factors (eg, lower cell dose for UCB units) may contribute to the longer LOS seen in black patients; however, the number of patients was too small for us to analyze an association between socioeconomic factors and LOS within each racial/ethnic subgroup.

This study has some limitations. Patients were treated at numerous different centers using various conditioning and GVHD prophylaxis regimens. We restricted our study to patients with acute leukemia in first or second CR or CR and to commonly used conditioning and GVHD prophylaxis regimens, to establish a relatively homogenous cohort. We were not able to account for variations in transplantation center practices [32,33], which could influence the hospital LOS for patients. In addition, the CIBMTR does not collect information on caregiver and community support, which also may influence LOS. Only 4 patients underwent outpatient HCT without the need for hospital admission during the first 100 days. Our study was limited to patients who underwent transplantation in the United States. We were not able to consider patient payor type and quality of insurance coverage, which could affect LOS after transplantation; for example, hospital LOS has been shown to be longer in Medicaid patients in other medical situations [34]. Medicare patients may have additional pressure to limit LOS. We were not able to account for important pretransplantation cost and resource factors (eg, costs of graft acquisition). Also, our study focused on hospitalizations over the first 100 days post-transplantation and was not able to account for later hospitalizations and resource utilization. Chronic GVHD and relapsed disease incur significant costs to the health care system, but were beyond the scope of this study. For example, chronic GVHD may be less prevalent among UCB recipients compared with recipients of other graft sources [1,6], which in turn may be associated with lower long-term costs and resource needs.

In conclusion, we comprehensively examined the hospital LOS in the first 100 days post-transplantation in patients undergoing HCT from alternative graft sources. We found an extended LOS for recipients of all of these alternative graft

sources, and conclude that protocols to improve engraftment, decrease infection, and improve home monitoring need to be developed to decrease LOS. The use of double UCB grafts was not associated with shorter LOS. The use of UCB was associated with a longer LOS compared with the other alternative graft sources analyzed in both pediatric and adult patients. These data will aid transplantation providers and centers in understanding the expected resources needed to treat individual HCT recipients, develop strategies to reduce LOS, and select the graft source likely to have the best outcome and be the most cost-effective. Future studies are needed to elucidate factors that may account for differential LOS among alternative graft sources, such as rates of infection, GVHD and engraftment, and to address interventions to reduce the duration of hospitalization in general.

ACKNOWLEDGMENTS

We thank Yoshiko Atsuta, MD, PhD, for her review of the draft manuscript.

Financial Disclosure: The CIBMTR is supported by Public Health Service Grant/Cooperative Agreement U24-CA76518 from the National Cancer Institute, the National Heart, Lung and Blood Institute (NHLBI) and the National Institute of Allergy and Infectious Diseases; a Grant/Cooperative Agreement 5U01HL069294 from NHLBI and NCI; a contract HHSH234200637015 C with Health Resources and Services Administration (HRSA/DHHS); two Grants N00014-06-1-0704 and N00014-08-1-0058 from the Office of Naval Research; and grants from AABB; Allos, Inc.; Amgen, Inc.; Anonymous donation to the Medical College of Wisconsin; Astellas Pharma US, Inc.; Be the Match Foundation; Biogen Idec BioMarin Pharmaceutical, Inc.; Biovitrum AB; BloodCenter of Wisconsin; Blue Cross and Blue Shield Association; Bone Marrow Foundation; The Bailey Family Foundation; Terumo BCT Celgene; CellGenix Children's Leukemia Research Association; ClinImmune Labs; CTI Clinical Trial and Consulting Services; Eisai, Inc.; Genentech, Inc.; Genzyme Corporation; Histogenetics, Inc.; HKS Medical Information Systems; Hospira, Inc.; Kirin Brewery Co., Ltd.; The Leukemia & Lymphoma Society; Merck & Company; The Medical College of Wisconsin; Millennium Pharmaceuticals, Inc.; Miller Pharmacal Group; Milliman USA, Inc.; Miltenyi Biotec, Inc.; National Marrow Donor Program; Nature Publishing Group; Novartis Oncology; Oncology Nursing Society; Osiris Therapeutics, Inc.; Otsuka America Pharmaceutical, Inc.; Pall Life Sciences; Pfizer Inc; Schering Corporation; Sigma-Tau Pharmaceuticals; Soligenix, Inc.; StemCyte, Inc.; StemSoft Software, Inc.; Sysmex America, Inc.; Texas Instruments Inc.; Vidacare Corporation; ViraCor Laboratories; ViroPharma, Inc.; and WellPoint, Inc. The views expressed in this article do not reflect the official policy or position of the National Institutes of Health, the Department of the; Navy, the Department of Defense, or any other agency of the U.S. Government.

Conflict of interest statement: There are no conflicts of interest to report.

REFERENCES

1. Eapen M, Rocha V, Sanz G, et al. Effect of graft source on unrelated donor haemopoietic stem cell transplantation in adults with acute leukaemia: a retrospective analysis. *Lancet Oncol*. 2010;11:653-660.
2. Laughlin MJ, Eapen M, Rubinstein P, et al. Outcomes after transplantation of cord blood or bone marrow from unrelated donors in adults with leukemia. *N Engl J Med*. 2004;351:2265-2275.
3. Rocha V, Labopin M, Sanz G, et al. Transplants of umbilical-cord blood or bone marrow from unrelated donors in adults with acute leukemia. *N Engl J Med*. 2004;351:2276-2285.
4. Takahashi S, Ooi J, Tomonari A, et al. Comparative single-institute analysis of cord blood transplantation from unrelated donors with bone marrow or peripheral blood stem cell transplants from related donors in adult patients with hematologic malignancies after myeloablative conditioning regimen. *Blood*. 2007;109:1322-1330.
5. Peffault de Latour R, Brunstein CG, Porcher R, et al. Similar overall survival using sibling, unrelated donor, and cord blood grafts after reduced-intensity conditioning for older patients with acute myelogenous leukemia. *Biol Blood Marrow Transplant*. 2013;19:1355-1360.
6. Chen YB, Aldridge J, Kim HT, et al. Reduced-intensity conditioning stem cell transplantation: comparison of double umbilical cord blood and unrelated donor grafts. *Biol Blood Marrow Transplant*. 2012;18:805-812.
7. Eapen M, Rubinstein P, Zhang MJ, et al. Outcomes of transplantation of unrelated donor umbilical cord blood and bone marrow in children with acute leukaemia: a comparison study. *Lancet*. 2007;369:1947-1954.
8. Khera N, Zeliadt SB, Lee SJ. Economics of hematopoietic cell transplantation. *Blood*. 2012;120:1545-1551.
9. Preussler JM, Denzen EM, Majhail NS. Costs and cost-effectiveness of hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2012;18:1620-1628.
10. Majhail NS, Mau LW, Denzen EM, et al. Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large national private claims database. *Bone Marrow Transplant*. 2013;48:294-300.
11. Majhail NS, Mothukuri JM, Brunstein CG, et al. Costs of hematopoietic cell transplantation: comparison of umbilical cord blood and matched related donor transplantation and the impact of posttransplant complications. *Biol Blood Marrow Transplant*. 2009;15:564-573.
12. Majhail NS, Mothukuri JM, Macmillan ML, et al. Costs of pediatric allogeneic hematopoietic cell transplantation. *Pediatr Blood Cancer*. 2010;54:138-143.
13. Solh M, Brunstein C, Morgan S, et al. Platelet and red blood cell utilization and transfusion independence in umbilical cord blood and allogeneic peripheral blood hematopoietic cell transplants. *Biol Blood Marrow Transplant*. 2011;17:710-716.
14. Pasquini M, Wang Z. Current use and outcome of hematopoietic stem cell transplantation. CIBMTR summary slides, 2013. Available from: http://www.cibmtr.org. Accessed March 1, 2014.
15. Baker KS, Davies SM, Majhail NS, et al. Race and socioeconomic status influence outcomes of unrelated donor hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2009;15:1543-1554.
16. Ballen KK, Klein JP, Pedersen TL, et al. Relationship of race/ethnicity and survival after single umbilical cord blood transplantation for adults and children with leukemia and myelodysplastic syndromes. *Biol Blood Marrow Transplant*. 2012;18:903-912.
17. Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. *Biol Blood Marrow Transplant*. 2009;15:1628-1633.
18. Giralt S, Ballen K, Rizzo D, et al. Reduced-intensity conditioning regimen workshop: defining the dose spectrum. Report of a workshop convened by the Center for International Blood and Marrow Transplant Research. *Biol Blood Marrow Transplant*. 2009;15:367-369.
19. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53:457-481.
20. Saito AM, Cutler C, Zahrieh D, et al. Costs of allogeneic hematopoietic cell transplantation with high-dose regimens. *Biol Blood Marrow Transplant*. 2008;14:197-207.
21. Saito AM, Zahrieh D, Cutler C, et al. Lower costs associated with hematopoietic cell transplantation using reduced-intensity vs high-dose regimens for hematological malignancy. *Bone Marrow Transplant*. 2007;40:209-217.
22. Esperou H, Brunot A, Roudot-Thoraval F, et al. Predicting the costs of allogeneic sibling stem cell transplantation: results from a prospective, multicenter French study. *Transplantation*. 2004;77:1854-1858.
23. Jaing TH, Tsay PK, Yang CP, et al. Evaluation of readmission in children receiving allogeneic hematopoietic stem cell transplantation: an institutional experience. *Transplant Proc*. 2008;40:3643-3645.
24. van Agthoven M, Groot MT, Verdonck LF, et al. Cost analysis of HLA-identical sibling and voluntary unrelated allogeneic bone marrow and peripheral blood stem cell transplantation in adults with acute myelocytic leukaemia or acute lymphoblastic leukaemia. *Bone Marrow Transplant*. 2002;30:243-251.
25. Blommestein HM, Verelst SG, Huijgens PC, et al. Real-world costs of autologous and allogeneic stem cell transplantations for haematological diseases: a multicentre study. *Ann Hematol*. 2012;91:1945-1952.
26. Labopin M, Ruggeri A, Gorin NC, et al. Cost-effectiveness and clinical outcomes of double versus single cord blood transplantation in adults with acute leukemia in France. *Haematologica*. 2014;99:535-540.
27. Brunstein CG, Fuchs EJ, Carter SL, et al. Alternative donor transplantation after reduced intensity conditioning: results of parallel

phase 2 trials using partially HLA-mismatched related bone marrow or unrelated double umbilical cord blood grafts. *Blood*. 2011;118:282-288.
28. Majhail NS, Nayyar S, Santibanez ME, et al. Racial disparities in hematopoietic cell transplantation in the United States. *Bone Marrow Transplant*. 2012;47:1385-1390.
29. Majhail NS, Omondi NA, Denzen E, et al. Access to hematopoietic cell transplantation in the United States. *Biol Blood Marrow Transplant*. 2010;16:1070-1075.
30. Barker JN, Byam CE, Kernan NA, et al. Availability of cord blood extends allogeneic hematopoietic stem cell transplant access to racial and ethnic minorities. *Biol Blood Marrow Transplant*. 2010;16:1541-1548.
31. National Center for Health Statistics. *Health, United States, 2011: with special feature on socioeconomic status and health*. Hyattsville (MD): National Center for Health Statistics; 2012.
32. Loberiza FR Jr, Zhang MJ, Lee SJ, et al. Association of transplant center and physician factors on mortality after hematopoietic stem cell transplantation in the United States. *Blood*. 2005;105:2979-2987.
33. Majhail NS, Murphy EA, Omondi NA, et al. Allogeneic transplant physician and center capacity in the United States. *Biol Blood Marrow Transplant*. 2011;17:956-961.
34. Allen LA, Smoyer Tomic KE, Wilson KL, et al. The inpatient experience and predictors of length of stay for patients hospitalized with systolic heart failure: comparison by commercial, Medicaid, and Medicare payer type. *J Med Econ*. 2013;16:43-54.